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REMARKS/ARGUMENTS

Claims 42-73 and 80-91 are active in this application. Applicants note that Claims 90 and 91 are drawn to the elected invention and the Examiner's attention is directed to a similar claim, Claim 73, which is also directed to a method of producing a polypeptide. Support for the amendment to Claims 42 and 60 is found in the specification as originally filed. No new matter is added.

Applicants thank the Examiner for indicating allowable subject matter in this application. In view of the amendments submitted herein and the following remarks, Applicants request allowance of all pending claims.

The rejection of Claim 60 under 35 U.S.C. § 102(b) over Hunter et al. is respectfully traversed.

The portion of the sequence in Hunter et al (page 3961, Fig. 2), which the Examiner alleges anticipates Claim 60 corresponds to the first 29 amino acids or 87 nucleotides in length (3 nucleotides per each amino acid). In particular, the Examiner contends that the MKK portion of the sequence (or 9 nucleotides) would hybridize to SEQ ID NO:4 under the stringent conditions set forth in Claim 60 AND encode a peptide with signal secretion activity. Applicants disagree.

As is clear from the alignment illustrated below, the nucleotide sequence of Hunter and SEQ ID NO:4 do not have a high degree of structural homology. In fact, at best over the length of the 90 nucleotides, the two sequences share approximately 33% identity (32 identical nucleotides over 90 total nucleotides).

```
                    *         20        *         40        *         60
hunter  :  atgaagaaaaaattattttcattagttatagttagttcactttaaacggatgcctattatcacc  : 65
SEQ:4   :  atgaaaaaaattattcaaagtttactgtaatttttatgttttcatgttttgttattgttggagc  : 65
           ATGAA AAAA   TT      TT   T TA TT  T    TTT A          T  T   A C

                    *         80        *
hunter  :  aactttagtgtatgcaaatgatata  : 90
SEQ:4   :  aataagtccaatgaaagcaagtgca  : 90
           AA             A     T  A
```

Therefore, the sequence of Hunter et al would not be hybridize to SEQ ID NO:4, which requires high stringency conditions. As described in the specification on page 5, lines 13-15: "sequences which hybridise under stringent conditions and which thus have a high degree of structural homology with the sequence under consideration." Certainly, a nucleotide sequence with only 33% identity to SEQ ID NO:4 cannot have such a high degree of structural homology.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 42 and 44 under 35 U.S.C. § 102(e) over Fach et al. is respectfully traversed.

Fach et al. describes two vectors pMRP 109 and pMRP 126.

The pMRP 109 vector comprises a DNA amplified by PCR from the total DNA of CWC 254 strain with the primers p279 and p280, which were derived from a N-terminal protein sequence and an internal protein sequence (see col. 5, lines 29-34) . The sequence of the beta toxin portion cloned into pMRP109 is described in the sequence bridging cols. 4-6 and is identified as SEQ ID NO:9. In other words, the 5' primer (p279) used for amplification corresponds to the first ten amino acids of the protein (the N-terminal end) and as such the 5' end of the sequence amplified by Fach et al. corresponds to the beginning of the coding sequence but not beginning of the gene (see also, col.5, lines 39-41: "This DNA corresponds to the beginning of the beta toxin 2 gene and codes for the first 225 amino acids of the functional protein"). Therefore, the sequence contained in this vector does not comprise a promoter sequence located upstream of the coding region.

Similarly, the pPRP 126 vector does not describe a sequence having transcription promoter activity because the pMRP 126 vector comprises the 3' end of the β2 coding sequence (see col. 6, lines 1-2: "pMRP126 is a recombinant plasmid containing the end of the beta 2 gene).

With respect to Figure 4 of Fach et al. the sequences presented therein are a comparison of amino acid sequences of the β2 and β1 toxins (see col. 7) but does not refer to a sequence with transcriptional promoter activity. Therefore, taken in its entirety Fach et al. does not provide a description for a sequence from a clostridium strain that has transcriptional promoter activity. Withdrawal of this ground of rejection is requested.

The rejection of Claims 43(b), 44-59 and 61-73 under 35 U.S.C. § 112, first paragraph ("enablement") is respectfully traversed.

As amended herein, Claim 42(b) is amended to define the sequence as being from a Clostridium strain which hybridizes to a complement of SEQ ID NO:3 under stringent conditions. As described on page 5, lines 13-15 of the specification "sequences which hybridize under stringent conditions and which thus have a high degree of structural homology with a sequence under consideration." Further, the sequences that hybridize under these conditions must also have the requisite transcriptional promoter activity.

The specification describes:

- a strain of clostridium microorganisms from which nucleic acid can be isolated (page 17, line 18);
- SEQ ID NO:3 (Sequence Listing);
- high stringency conditions (page 5, lines 6-11);
- the requisite elements in an expression vector, e.g., origin of replication, marker genes, and multiple cloning signs (page 19);
- constructing a vector with the isolated nucleic acid upstream of a reporter gene, for example, LacZ (page 17, lines 29-30);
- transforming the cells, e.g., via electroporation (page 20, lines 27-28);
- host cells that are suitable for transformation, for example, *Clostridium perfringens* (page 17, lines 27-28); and

- guidance to determine that the purified nucleic acid encoded by the sequence provides transcriptional promoter activity (page 17, lines 24-26).

Accordingly, in view of the extensive guidance provided in the specification, it would not require undue experimentation to make and/or use the claimed invention, i.e., in Claim 42, subpart (b). Withdrawal of this ground of rejection is requested.

For similar reasons, the rejection of Claims 60, 81, 83, 85, 87 and 89 under 35 U.S.C. § 112, first paragraph ("enablement") is respectfully traversed.

First, contrary to the Examiner's statement on page 6, the claims clearly stated that the polynucleotides encodes a peptide that functions as a secretion signal peptide (see the last clause of Claim 60).

Second, as noted above, the specification provides extensive guidance with respect to the stringent conditions, microorganisms, SEQ ID NO: 4, the requisite elements in an expression vector, construction of vector, and the transformation of cells.

Third, with respect to the ability of a peptide to function as a secretion signal, the Examiner's attention is drawn to the specification on page 18, lines 24-31 that provides details for determining whether a peptide functions as a secretion signal peptide. Furthermore, specific examples of this are also provided in the examples on pages 19-22.

Accordingly, in view of the extensive guidance provided in the specification, it would not require undue experimentation to make and/or use the invention claimed in Claim 60. Withdrawal of this ground of rejection is requested.

The objection to Claim 2 is addressed by amendment.

Applicants request allowance of this application.

Respectfully submitted,

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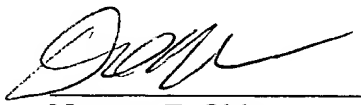

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